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APPLICATION NO. 057722-018	FILING DATE 11/23/96	SEED FIRST NAMED INVENTOR	ATTORNEY DOCKET NO. 00786/284002
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GAMBEL, P.  
EXAMINER

1644  
ART UNIT PAPER NUMBER  
12/29/98

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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EXAMINER

ART UNIT

PAPER NUMBER

13

DATE MAILED:

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

- ☒ Responsive to communication(s) filed on 10/19/98
- ☐ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-23 is/are pending in the application.
- Of the above, claim(s) 1-9, 11, 15-23 is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 10, 12-14 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

Application Papers

- ☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☒ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449. Paper No(s). \_\_\_\_\_
- ☐ Interview Summary, PTO-413
- ☒ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

- SEE OFFICE ACTION ON THE FOLLOWING PAGES -

#### DETAILED ACTION

1. The location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1644, Technology Center 1600.

2. Applicant's amendment, filed 10/19/98, is acknowledged.  
Claims 10 and 12 have been amended.

Claims 10, 12-14 as it applies to antibody domains are under consideration.

Claims 1-9, 11 and 15-23 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention and species.

3. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84.  
Please see the enclosed form PTO-948.

Applicant is reminded to change the Brief Description of the Drawings in accordance with these changes (see Views).

4. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.  
This Office Action will be in response to applicant's arguments, filed 10/19/98 (Paper No. 12).  
The rejections of record can be found in the previous Office Action (Paper No. 10).

5. Claims 10 and 12-14 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "artificial P-selectin ligand, wherein said polypeptide contains an amino acid consensus sequence for attachment of a sialyl Le<sup>x</sup> moiety and an amino acid consensus sequence for attachment of a sulfate moiety and wherein at least one of the consensus sequences is located at an amino acid position in said polypeptide which is different from its position in a naturally-occurring P-selectin ligand".

Applicant's reliance on page 24 and 28 of the specification is acknowledged. However, the term "artificial" does not appear in these sections of the specification. Further, the limited disclosure of sites or repeat sequences from Factor VIII, the fourth component of complement, PSGL-1 or CD43 does not provide for the broader recitation of consensus sequences encompassed by the amended claimed recitation.

The specification as filed does not appear to provide a written description or set forth the metes and bounds of "artificial P-selectin ligand" and the two "consensus sequences". The specification does not provide sufficient landmarks nor direction for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. The failure to meet the written description requirement under 35 USC 112, first paragraph arises when the claims are changed after the filing date to change the scope of the disclosure, which does encompass setting forth subgeneric claims (see MPEP 2163.05). Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action  
Alternatively, applicant is invited to provide for the written description of the amended limitations in the specification as filed.

6. Claims 10 and 12-14 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite in the recitation of "artificial P-selectin ligand, wherein said polypeptide contains an amino acid consensus sequence for attachment of a sialyl Le<sup>x</sup> moiety and an amino acid consensus sequence for attachment of a sulfate moiety and wherein at least one of the consensus sequences is located at an amino acid position in said polypeptide which is different from its position in a naturally-occurring P-selectin ligand" because the characteristics of the "artificial P-selectin ligand" and the "consensus sequences" are ambiguous and unclear. For example, page 24 of the specification discloses "synthetic" ligands, but not "artificial" ligands. Also, page 24 of the specification provides for the limited disclosure of sites or repeat sequences from Factor VIII, the fourth component of complement, PSGL-1 or CD43; but does not provide for the broader recitation of consensus sequences encompassed by the amended claimed recitation. This amended claim language is vague and indefinite since it encompasses a myriad of different "artificial ligands" and "consensus sequences" and it is not apparent from the disclosure which particular "artificial ligands" and "consensus sequences" are being referred to. While there appears some notion of function (e.g. P-selectin ligand, attachment of moieties); there is insufficient biochemical information (e.g. sequence, etc.) that distinctly identifies the "P-selectin ligand" and "consensus sequences", encompassed by the claimed invention. The recitation of "artificial ligands" and "consensus sequences" fails to distinctly claim what that polypeptide is and what the compositions are made up of. Therefore, there is insufficient information and guidance for the metes and bounds of "artificial ligands" and "consensus sequences".

There is insufficient direction or guidance provided to assist one skilled in the art in the selection of such "artificial ligands" and "consensus sequences" nor is there sufficient evidence provided that such "artificial ligands" and "consensus sequences" could be used in a practical manner as P-selectin ligands. It would require undue experimentation to produce all such possible "artificial ligands" and "consensus sequences" without more explicit guidance from the disclosure. It would require undue experimentation to investigate all such "artificial ligands" and "consensus sequences". It is readily apparent what is the scope of "artificial ligands" and "consensus sequences" encompassed by the claimed invention. Applicant has failed to enable or provide written description for nucleic acids encoding a myriad of "artificial ligands" and "consensus sequences" and fails to provide any guidance to those skilled generally on how to make and use useful nucleic acids encoding such a myriad of "artificial ligands" and "consensus sequences". Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. It appears that undue experimentation would be required of one skilled in the art to practice the claimed nucleic acids that encode said "artificial ligands" and "consensus sequences" commensurate in scope with the claimed invention using the teaching of the specification alone.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

7. Upon reconsideration of applicant's amended claims and arguments, filed 10/19/98; the previous rejections under 35 U.S.C. § 102(b)(e) and 35 U.S.C. § 103 have been withdrawn.

8. Claims 10 and 12-14 are rejected under 35 U.S.C. § 103 as being unpatentable over Larsen et al. (U.S. Patent No. 5,843,707) OR Sasaki et al. (J. Biol. Chem., 1994; 1449) OR Sako et al. (Cell, 1993) in view of Aruffo et al. (Cell, 1991) and Lowe et al. (U.S. patent No. 5,595,900).

Larsen et al. Teach nucleic acids encoding P-selectin ligands, including modified and altered forms thereof as well as the importance of carbohydrate and sulfation sites in selectin-mediated binding and structure (see entire document).

Sasaki et al. teach selectin ligands that have been modified to express carbohydrate moieties, as well as the nucleic acid, vector and cells that encode and express said modified ligands.

Sako et al. Teach nucleic acid encoding P-selectin ligand as well as the importance of carbohydrate sites in selectin-mediated binding and structure (see entire document).

The primary references differ from the instant claims by not providing for sulfation and sialyl Le<sup>x</sup> sites at non-naturally occurring sites in nucleic acids encoding P-selectin ligands.

In addition to the teaching of Larsen et al. on the importance of sulfation sites (see columns 8-9, overlapping paragraph, for example); Aruffo et al. Also teach the importance of sulfation sites for P-selectin binding by suppressing P-selectin binding via the sulfation suppression (see entire document). Therefore, it was known at the time the invention was made that both sialyl and sulfation sites and structures contributed to P-selectin binding.

Given the importance of both sialyl and sulfation moieties to the affinity and avidity of P-selectin-mediated binding, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide such moieties to modified/altered P-selectin ligands. It is noted that Larsen et al. teach nucleic acids encoding various modified/altered P-selectin ligands, including fragments and fusion proteins thereof for various uses (see columns 8-18). Lowe et al. teach providing nucleic acids that encode for glycosylation and sulfation sites in glycoproteins of interest (see column 14, paragraph 2, for example). Therefore, the ordinary artisan would have motivated and would have expected the provision for sialyl and sulfation sites at non-naturally occurring sites in the generation of various modified/altered P-selectin ligands either to provide for or to increase affinity/avidity of such molecules. For convenience and homogeneity, it would have obvious to provide such sites in the nucleic acids encoding said altered/modified P-selectin ligands. Given the convenience of such, it would have been obvious to the recognized the art-known importance of carbohydrates in such receptor-ligand interactions.

In addition, it would have been obvious to the ordinary artisan to provide such modifications encompassing sialyl Le<sup>x</sup> determinants or sulfated determinants to affect receptor-ligand interactions in characterizing structure-function relationships between such receptor-ligand interactions as well as their use to modify such receptor-ligand interactions.

One of ordinary skill in the art at the time the invention was made would have been motivated to select nucleic acids encoding artificial P-selectin ligands including immunoglobulin fusion proteins and to modify the expression of sialyl Le<sup>x</sup> determinants and sulfated determinants on said organic molecules to evaluate their effects in receptor-ligand interactions as well as to regulate said interactions. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.  
Patent Examiner  
Group 1640  
Technology Center 1600  
December 28, 1998

*Phillip Gambel*